Evaluation of sex-dependent kidney oxidative stress response to ochratoxin A in F344 rats using the comet assay in combination with FPG

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Ochratoxin A (OTA) is a secondary fungal metabolite that contaminates a great variety of foodstuffs. It is nephrotoxic in all animal species tested, considered a potent renal carcinogen in rodents and proposed as a possible etiological agent of the Balkan Endemic Nephropathy (BEN) in humans. Indeed, the International Agency for Research on Cancer (IARC) has classified OTA as a possible human carcinogen (group 2B). Its mechanism of action is still unknown, although oxidative stress appears to play an important role. Besides, large sex-differences have been observed in different carcinogenicity studies towards OTA-induced renal tumours.

Therefore, the objective of this study was to evaluate the sex-dependent kidney oxidative stress response to OTA in F344 rats. For that purpose, male and female F344 rats were administered by oral gavage with bicarbonate or 0.5 mg OTA/kg b.w. for 7 days, or with bicarbonate, 0.21 mg OTA/kg b.w. or 0.5 mg OTA/kg b.w. for 21 days. As this genotoxicity study was embedded in a bigger general toxicology study, the kidney samples for the comet assay were flash frozen by immersion in liquid nitrogen and stored at -80 °C until analysis. Therefore, the freezing and thawing processes of the kidney samples were also set up. The standard alkaline comet assay was used in combination with formamidopyrimidine DNA glycosylase (FPG), which detects oxidised bases.

The preliminary results of kidney samples of animals treated for 7 days will be presented. Taking into account these results, we are not able to conclude that ochratoxin A induces either single or double DNA strand breaks, or an increase of DNA oxidative damage following a sex-dependent pattern.